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Structure/Function Studies of UDP-N-Acetylglucosamine 1-Phosphate

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ABSTRACT: The *E. coli* (UDP-N-acetylglucosamine 1-Phosphate Uridyltransferase (GlmU) is a bifunctional enzyme that catalyzes acetylation of glucosamine-1-phosphate and subsequent condensation of *N*-acetylglucosamine-1-phosphate with UTP to form pyrophosphate and the activated sugar, UDP-GlcNAc. UDP-GlcNAc is the fork metabolite between bacterial lipopolysaccharide and peptidoglycan biosynthesis. GlmU is a member of the hexapeptide acyltransferase superfamily of enzymes that share a common structural domain termed a left-handed beta helix. Enzymes of this superfamily may represent attractive targets for drugs directed against microbial pathogens since they are frequently essential for bacterial viability and do not have mammalian homologs. We seek to determine the x-ray crystal structure of a number of complexes of ligands with GlmU that are bound to either the acetyltransferase or pyrophosphorylase active sites. Such complexes will identify important active sites residues, reveal catalytically essential conformational changes and may permit more general conclusions to be drawn concerning the mechanism of action of other hexapeptide acyltransferases.